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Familial Transient Global Amnesia

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Key Words

Transient global amnesia · Familial occurrence · Migraine

Abstract

Following an episode of typical transient global amnesia (TGA), a female patient reported similar clinical attacks in 2 maternal aunts. Prior reports of familial TGA are few, and no previous account of affected relatives more distant than siblings or parents was discovered in a literature survey. The aetiology of familial TGA is unknown. A pathophysiological mechanism akin to that in migraine attacks, comorbidity reported in a number of the examples of familial TGA, is one possibility. The study of familial TGA cases might facilitate the understanding of TGA aetiology.

Introduction

The syndrome of transient global amnesia (TGA), first described as such by Fisher and Adams [1] in 1964, is characterised by abrupt and temporary (<24 h) disruption of anterograde memory without clouding of consciousness or focal neurological signs. Patients typically present with repetition of the same questions or statements, followed by full recovery but without memory for the amnesic period [2].

The pathophysiology of TGA is uncertain, but probably involves transient hypoperfusion of memory-eloquent brain structures including the medial temporal lobe and hippocampus, as evidenced by sophisticated neuroimaging studies [3]. Despite its sudden onset, there is no evidence for an epileptic aetiology in TGA [4], although misdiagnosis as epilepsy or stroke by clinicians unfamiliar with TGA is not uncommon [5]. A possible relationship to migraine, particularly in younger patients, has been noted [6]. Familial cases of TGA have rarely been reported [7–12].

We present further familial TGA cases, survey prior publications on this topic, and consider the possible aetiology of familial TGA.

Case Presentation

A 54-year-old female had an episode of neurological disturbance of about 2.5 h duration after taking her dog for a walk. An eyewitness of the attack reported that the patient was repeatedly asking the same questions. She had little recollection of the episode after recovery but had a vague recollection of being fearful. There was no prior history of similar episodes. She had a mild migraine tendency but was otherwise in good health and took no regular medication. There was no history of temporal lobe auras. Neurological examination 1 month after the event was normal. As the patient was well, no further investigation (brain MRI, Dopplers, EEG and blood tests for stress hormones) was undertaken. Based on the history, proposed diagnostic criteria for TGA [2] were felt to be fulfilled.

The patient reported that in the family history, 2 maternal aunts had had similar symptoms at similar ages to herself and had both been diagnosed with TGA. It was not disclosed whether these individuals also had migraine. The patient's mother had died at a young age.

Discussion

Most cases of TGA are sporadic. Familial occurrence of TGA has been reported on occasion ([table 1](#)) [7–12], but all prior reports have involved siblings, with only occasional definite [8] or possible [12] instances of parental involvement. Prior accounts of familial involvement with more distant relatives, as in the current report, have not been identified.

Summing all the 22 patients in these 7 reports, there is a slight female preponderance (F:M = 14:8), with all episodes occurring in the 6th–8th decades of life. Although details are incomplete, at least 6 of these individuals (5 F, 1 M) had a history of migraine, and 1 patient had migraine-type headaches immediately after two TGA episodes [10].

Typical precipitating factors for TGA (physical exercise and emotional upset) were recorded in 13/22 familial cases. No details on whether our patient had undertaken strenuous physical exertion whilst walking her dog were available.

What might be the aetiology of familial TGA? Some clinicians are of the view that 'TGA is probably a migraine aura in most cases' [13], in which case a familial tendency to TGA would not be surprising. Likewise, a female preponderance of cases, as noted in some prior surveys of TGA [6, 14], might be deemed consistent with a migrainous aetiology. Comorbidity with migraine has been noted in some of the reports of familial TGA [9, 10], but only in some family members in other reports [12] or not at all [7]; still other reports make no comment on migraine [8, 11]. Since migraine is a highly prevalent condition, it cannot be assumed that the presence of this variable necessarily influences the occurrence of TGA.

Recognised triggers of TGA include physical exertion [6], which may also trigger migraine attacks. It may be that in some families, a genetically determined migraine tendency may also predispose to attacks of TGA [12]. If this were the case, then it is perhaps surprising that familial TGA is so rare when migraine is so common. Other genetically influenced developmental factors, perhaps related to local blood vessel structure or innervation, which rendered the hippocampal blood supply particularly vulnerable, might predispose only certain families.

Though apparently rare, familial TGA cases might facilitate the understanding of TGA aetiology. If routine questioning of all TGA patients about a family history of similar events proved positive, then these patients might be submitted to further investigation (brain MRI, Dopplers, EEG and blood tests for stress hormones) to address the proposed TGA aetiologies.

Table 1. Summary of accounts of familial TGA

Reference	TGA patient details	Migraine history
Corston and Godwin-Austen, 1982 [7]	4 male siblings, 2–3 attacks each when they were in their 60s and 70s. 3 of 4 had TGA attacks in context of exercise	none
Munro and Loizou, 1982 [8]	2 siblings (1 F, 1 M) and their father, 1–3 attacks in their 50s and 60s	not commented on
Stracciari and Rebucci, 1986 [9]	2 siblings (1 F, 1 M), attacks in their 70s and 50s, respectively; latter associated with exercise on a windy day	both had a history of migraine; F until menopause, M in adolescence
Dupuis et al., 1987 [10]	Twin sisters (probably monozygotic), 2 and 1 attacks, respectively, in their 60s	both migraineurs since adolescence; both attacks in first sister followed by severe migraine
Agosti et al., 2007 [11]	3 female siblings in their 60s, attacks following emotional upset, cold shower, and sexual intercourse, respectively	not commented on
Segers-van Rijn and de Bruijn, 2010 [12]	4 siblings (3 F, 1 M) and possibly their mother, attacks after exercise (3) and air travel (1), and on birthday; attacks between their 50s and 70s	one of the female siblings had a history of migraine with aura
Davies and Larnar, 2012 [present report]	Female and 2 maternal aunts, attacks in their 50s and/or 60s, after exercise in the index case	migraine in the index case, no information on other cases

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